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Diffusional Contributions and Electrostatic Exclusion Effects on Transport through Ultrafiltration Membranes

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1. Introduction

Ultrafiltration is used for protein concentration and buffer exchange in the downstream processing of essentially all recombinant protein products [1]. Although ultrafiltration has traditionally been viewed as a convective pressure-driven process, with the separation determined on the basis of size, solute transport through ultrafiltration membranes is also strongly influenced by solute diffusion and electrostatic interactions [2, 3]. Electrostatic interactions can be exploited for high-resolution protein separations, taking advantage of the unique surface charge characteristics of individual proteins. Diffusional transport in ultrafiltration not only influences the separation characteristics, it also provides a directional dependence to solute transport through typical asymmetric ultrafiltration membranes [4].

2. Electrostatic Interactions

Solute transport in ultrafiltration is governed by both thermodynamic and hydrodynamic interactions. The charged protein and the charged surface of the membrane pore are both surrounded by an electric double layer, the region of space in which the protein / membrane charge is balanced by an excess concentration of counterions. The entrance of the protein into the pore causes a deformation (or distortion) of electrical double layers (see Figure 1), causing an increase in the free energy of the system reducing the protein concentration within the pore and thereby decreasing the overall rate of protein transport.

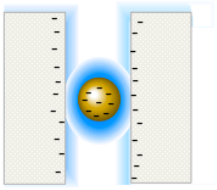

Figure 1: Schematic diagram of electrical double layer deformation in membrane pore

Smith and Deen [5] developed the first rigorous analytical expressions for the electrostatic potential for a spherical solute in a cylindrical pore by solving the linearized Poisson-Boltzmann equation using matched asymptotic expansions in cylindrical and spherical coordinates. The results for interactions at constant surface charge density are conveniently expressed as:

$$\frac{\psi_E}{k_B T} = A_s \sigma_s^2 + A_{sp} \sigma_s \sigma_p + A_p \sigma_p^2 \qquad (1)$$

where σ_s and σ_p are the dimensionless surface charge densities of the solute (protein) and pore and the coefficients A_s, A_p, and A_{sp} are functions of the protein and pore radii and the solution ionic strength. The first term in Equation (1) represents the increase in electrostatic energy of interaction associated with the deformation of the electrical double

layer around the protein while the last term represents the energy associated with the deformation of the electrical double layer adjacent to the pore wall. The middle term describes the direct charge-charge interactions and is positive (i.e., repulsive) when the protein and pore have like polarity.

Recent experimental studies [6] have demonstrated that it is possible to control the extent of electrostatic interactions by appropriate modification of the pore surface using ligands with specific charge functionality. For example, novel high performance ultra-filtration membranes can be produced by chemical modification of cellulose membranes using ligands that have multiple amine groups, leading to very high local surface charge densities. The length, chemical structure, and charge density of the ligand can all be chosen to enhance the performance of ultrafiltration membranes for given applications.

3. Diffusional Transport

Almost all commercial ultrafiltration membranes have an asymmetric structure in which a very thin permselective "skin" is supported on a macroporous substructure that provides the membrane with the required mechanical stability. The overall rate of solute transport through these asymmetric structures is determined by the detailed properties and the orientation of the two layers. Solute transport is enhanced when the fluid flow occurs through the substructure and towards the skin due to internal concentration polarization that develops within the membrane substructure in this orientation. The extent of this internal polarization is governed by the effective solute diffusion coefficient within the substructure. Experimental and theoretical studies demonstrate that appropriate composite membrane structures can have higher selectivities than homogeneous membranes [4]. In addition, multilayer membranes can be designed to control the directional transport rates through these structures. The implications of these transport phenomena are examined in several different ultrafiltration applications.

4. Conclusions

High performance ultrafiltration membranes have been developed by exploiting electrostatic interactions between charged proteins and surface-modified membranes. These membranes can be used to separate proteins with very similar size and properties, providing exciting new opportunities for ultrafiltration in the downstream processing of high-value biotherapeutics. Proper control of these processes requires an understanding of the combined effects of diffusion and convection on protein transport in porous membranes.

References

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